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Case report

A forensic autopsy case of death in a patient with pseudoxanthoma elasticum – Dermatopathologic findings as a clue of the cause of death

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ABSTRACT

Pseudoxanthoma elasticum (PXE) is an autosomal recessive disorder, characterized by papular skin lesions and cutaneous laxity caused by fragmentation and mineralization of elastic fibers. Although vascular and retinal aspects of this disease and their associated complications are well characterized, few authors have focused on the increased incidence of epilepsy in patients with PXE. A 28-year-old Korean male was found dead in his work place with bloody-foamy discharge from his mouth and nostrils. He reportedly had a convulsive episode 5 days prior to his death in the work place. The skin showed generalized laxity and many creases with maculopapular pigmentations. A histopathologic examination of the skin revealed Pseudoxanthoma elasticum. Based on the histopathological findings and medical history, death was postulated to be due to 'an internal cause, possibly related to a seizure attack'. Our findings suggest that histopathologic examinations of any lesions found during the forensic autopsy should be encouraged.

1. Introduction

Although dermatologic diseases are unlikely to be related to the cause of death and are, therefore, frequently overlooked during forensic autopsies, dermatopathologic analyses of forensic specimens can sometimes provide valuable information as we will demonstrate in this case report. We encourage histopathologic examination of any dermatological lesions found during the autopsy to prevent overlooking important findings.[1] To illustrate our point, we present an autopsy case, in which we suspect that death was related to one of the possible neurological complications of a dermatological disorder, pseudoxanthoma elasticum (PXE).

2. Case report

A 28-year-old Korean male was found dead in his work place by his colleagues. The deceased was in a prone position with bloody-foamy discharge from the mouth and nostrils. The deceased had joined the construction company as a concrete intensity examiner 2 months prior to his death. Although the family of the deceased denied that he had any medical problems, one of his colleagues reported that the deceased had shown convulsive symptoms just 5 days prior to his death. Previous medical records provided by the National Health Insurance Corporation revealed that the deceased had visited different clinics three times due to an unspecified neurological problem or convulsive disorder during recent 2 years. The detailed medical records were not available because of privacy agreement of the clinics.

Upon inspection, the skin showed generalized laxity and many creases, but no trauma. The skin had a leathery, thick appearance,

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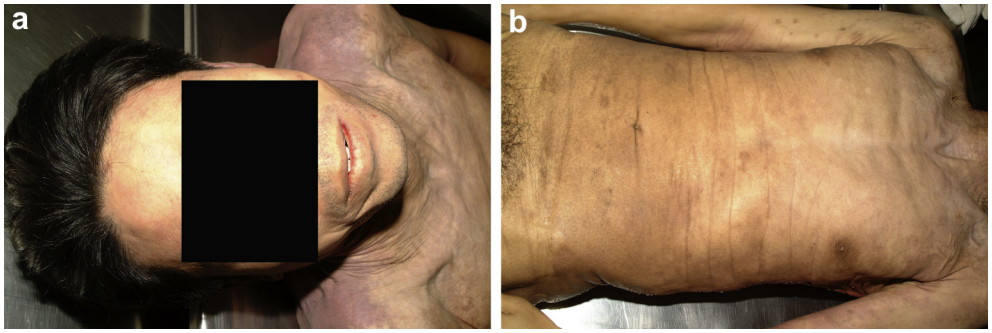

Fig. 1. Generalized laxity with many creases was noted in the skin. Maculopapular pigmentations were also observed (in the right arm).

with maculopapular pigmentations mainly on the skin of the thighs, calves, and shoulders (Fig. 1). In the autopsy room, atopic dermatitis, which is quite common in the Korean population, was initially suspected. Internal examination of vital organs, such as the brain, heart, lung, liver, and kidneys, failed to reveal any possible cause of death. Atherosclerotic lesions were not found in the coronary arteries or major cerebrovascular structures or cardiac valves by either gross or microscopic examinations. Histopathological investigation of the skin revealed hyphae-like calcified basophilic fibers in the dermis, consistent with PXE (Fig. 2). However, vascular involvement of PXE was not noted in any organs, including the brain and heart. On gross examination of the brain, the pattern of gyri and sulci was within normal limits. Serial coronal section through the cerebrum revealed neither structural anomaly nor mass-like lesions including necrosis with well demarcated gray-white matter junction. The both hippocampus looked normal in size. A routine histopathologic examination of the brain parenchyma was unremarkable. Full toxicological examinations, including blood carboxyhemoglobin and narcotics, produced only negative results. Because any external cause of death could be excluded by the autopsy and laboratory examinations, the manner of death was concluded to be a death due to an internal cause. A possibility of epilepsy and possible association of epilepsy and PXE were suggested in the final autopsy report.

3. Discussion

PXE is an autosomal recessive disorder, characterized by small, yellowish papular skin lesions and cutaneous laxity caused by fragmentation and mineralization of elastic fibers.[2] Mutations in the ABCC6 gene are responsible for the development of this disease.[3] The prevalence of PXE is about 1 in 25,000 to 100,000 with two-fold preponderance in female.[4] Favored cutaneous sites of involvement are the neck, axillae, groin, and intertriginous areas. The skin of patients with PXE cutaneous involvement is characterized by laxity, redundancy, and many oblique creases.[5] Derangement of elastic fibers occurs not only in the skin, but also in other tissues, such as the eyes and arteries.[5] Vascular involvement of this disease can cause a variety of complications, including coronary arterial pathology and cerebrovascular accidents.[6,7] Occasionally, ocular involvement can result in retinal hemorrhage and blindness.[5,8] Many complications of PXE, such as intracerebral hemorrhage,[9] cerebral infarct,[10] myocardial infarct,[11,12] cardiac valve pathology,[13] and gastrointestinal bleeding[14] can cause sudden death.[15] However, to the best of our knowledge, there has been no report of death due to PXE-related epilepsy.

The reported incidence of epilepsy in PXE patients ranges from 1.5% (3 in 200 cases) according to Eddy and Farber[16] to 2.8% (3 in 106 cases) based on a study by Connor and colleagues.[17] Goto described a 23-year-old Japanese woman with PXE who experienced chronic convulsive seizures.[18] Because Goto's patient had a completely obstructed left internal carotid artery, her left middle cerebral artery was supplied by the posterior and anterior communicating arteries. Aneurysmal dilatations at the basilar and the left ophthalmic arteries were also observed in Goto's patient. Although Goto did not relate the cerebral vascular lesions to epilepsy, it can be hypothesized that focal or global cerebral ischemia due to vascular involvement of PXE may be epileptogenic. Davis et al. reported a rapid visual loss due to angioid streaks of PXE in a 41 year-old male patient, who had a 25 year history of grand mal epilepsy.[19] Surprisingly, despite the increased incidence of epilepsy,[17] the mechanism of epilepsy in PXE has not yet been clearly demonstrated. Bonkowsky et al. even denied any

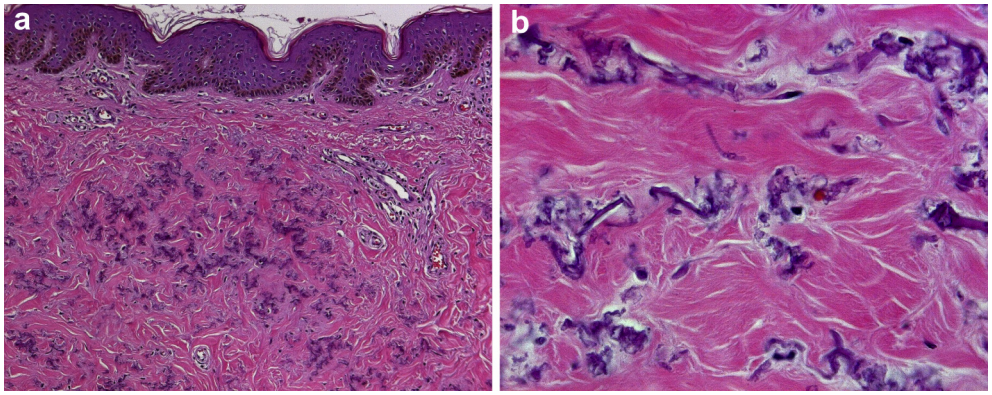

Fig. 2. Histopathologic examination (Hematoxylin and eosin stain) of the skin revealed hyphae-like calcified basophilic fibers intermingled in the collagen bundles of the dermis, consistent with pseudoxanthoma elasticum.

relationship between epilepsy and PXE, although they did not provide any evidence to support this claim.[20] Interestingly, in the case of Marfan's syndrome, another genetic disease involving elastic fibers and producing angioid streaks, the incidence of epilepsy is also increased, although the mechanism is not well understood yet.[21] Because there is no satisfactory explanation for the increased incidence of epilepsy in PXE, further researches are required.

The present case demonstrates that dermatopathologic examination of forensic autopsy specimens may help estimate the cause of death and may indicate the need for genetic counseling of family members. Therefore, we strongly encourage dermatopathologic approaches to skin lesions encountered at autopsy.

Ethical approval

It was not necessary.

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Conflict of interest

None.

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